

CLAIMS

1°) An isolated and purified peptide, characterized in that it has the following formula:

X1-X2-X3-X4-X5-X6-X7-X8-X9,

5 wherein:

X1 is absent or represents an amino acid selected in the group consisting of non-charged polar amino acids and non-polar amino acids,

X2 is absent or represents an amino acid selected in the group consisting of acidic amino acids, non-charged polar amino acids and non-polar amino acids,

10 X3 is selected in the group consisting of basic amino acids, non-charged polar amino acids and non-polar amino acids,

X4 is W,

X5 represents any amino acid except A, L or I,

15 X6 is a non-polar amino acid,

X7 is a basic amino acid

X8 is selected in the group consisting of basic amino acids and non-charged polar amino acids and

20 X9 is absent or represents an amino acid selected in the group consisting of basic amino acids and non-polar amino acids.

2°) The isolated peptide according to claim 1, characterized in that it is selected in the group consisting of peptides of 6-9 amino acids wherein X5 represents F.

3°) The isolated peptide according to claim 1 or to claim 2, characterized in that said peptide is associated with or conjugated to another peptide or protein such as a carrier protein or non-peptide molecule and/or incorporated into a suitable support.

4°) Attenuated flavivirus strains, which include the nucleotide sequences encoding the peptides according to claims 1 or 2, with the proviso that said attenuated flavivirus strain is different from the Yellow fever strains having the following GENPEPT accession numbers: AF052437, AF052438, AF052439,

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AF052440, AF52442, AF052444, AF052445, AF052446, AF052447, AF094612, X03700, U17066, U17067, U21055, X15062.

5°) Attenuated dengue virus strains, which include the nucleotide sequences encoding the peptides according to claims 1 or 2.

5 6°) Attenuated flavivirus strains according to claim 5, characterized in that they correspond to DEN-2 strains.

7°) Isolated and purified polynucleotide, characterized in that it encodes a peptide according to any of claims 1 and 2 or attenuated flavivirus strain according to claims 4 to 6.

10 8°) Recombinant vector, characterized in that it comprises a polynucleotide according to claim 7.

9°) Recombinant vector according to claim 8, characterized in that it contains a polynucleotide encoding an attenuated flavivirus strain including the polynucleotide sequence encoding a peptide according to claims 1 or 2 and more specifically encoding a peptide in which X5 = F.

15 10°) Recombinant vector according to claim 9, wherein it corresponds to plasmid [95-114]EGFP[M1-M40] (I36F) DEN-2 which has been deposited at the Collection Nationale de Cultures de Microorganismes, 28 Rue de Docteur Roux, F-75724 Paris Cedex 15, on June 25, 2003 under the number I-3061

20 11°) Host cell, characterized in that it is transformed by a recombinant vector according to anyone of claims 8 to 10.

12°) Polyclonal or monoclonal antibodies raised against a peptide of claims 1 to 3 or an attenuated flavivirus strain according to claims 4 to 6.

25 13°) Pharmaceutical composition comprising an effective amount, for inducing protection against flavivirus infections, of a peptide according to claims 1 to 3 or a polynucleotide encoding the same or a polynucleotide encoding an attenuated flavivirus strain according to claims 4 to 6, and at least one pharmaceutically acceptable carrier.

30 14°) An immunogenic composition able to protect against a flavivirus infection comprising a modified DEN-2 strain of flavivirus, wherein the sequence encoding the M protein comprises in position 241 a codon for any amino acid residue except A, L or I.

15°) Use of the peptide according to claims 1 to 3, the polynucleotide of claim 7 or the recombinant vector according to claims 8 to 10 for the preparation of a medicament for the prevention and/or the treatment of pathological conditions from non-specific febrile illnesses to severe hemorrhagic manifestations, encephalitic syndromes, these pathological conditions being linked to Flavivirus infection or cancers.

16°) Method for the preparation of attenuated strains of flavivirus wherein said attenuation is obtained by expression of a mutated M ectodomain protein of said flavivirus, in which the amino acid sequence between positions 237-245 of said M ectodomain protein, in reference of the DEN-1 M ectodomain is a peptide according to claim 1.

17°) Method for the preparation of attenuated strains of flavivirus wherein said attenuation is obtained by expression of a mutated M ectodomain protein of said flavivirus, in which the amino acid sequence between position 237-245 of said M ectodomain protein, in reference of the DEN-1 M ectodomain is a peptide according to claim 2.

18°) Direct detection method of a flavivirus infection, characterized in that it comprises:

- contacting a biological sample to be analysed or a culture medium supposed to eventually contain flavivirus antigens with antibodies according to claim 12, optionally labelled and,
- detecting the antigen-antibody complex eventually formed by any means.

19°) Serological detection of a flavivirus infection, characterized in that it comprises:

- contacting a biological sample with a solid support on which peptides according to claims 1 or 2 are bound, and
- detecting the eventually formed antigen-antibody complexes by any means.

20°) A method for the vaccinal survey of a patient, comprising the detection in a biological fluid of said patient of antibodies directed against an attenuated flavivirus strain according to claims 4 or 5.

21°) Chimeric flavivirus, wherein the M ectodomain includes a peptide according to claims 1 or 2.